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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/216,506	03/22/1994	C. RICHARD SCHLEGEL	010091001	8196

909 7590 03/18/2009

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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
03/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/216,506	SCHLEGEL ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/22/07, 9/10/07, 11/15/06* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *67-91* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :6/10/93, 6/3/94, 6/6/94, 3/14/95.

DETAILED ACTION

Interference

Interference No. 104,776 has been terminated by a decision adverse to applicant. *Ex parte* prosecution is resumed.

Prior to the interference, claims 1-3, 12-14, 16, 19, 23-25, 46, 47, 50, 52, 53, 55-60, 62, and 64 were held allowable. Claim 61 was rejected as indefinite because of the recitation "…L1 protein does not comprise virus-like particles." Claims 10, 11, 15, 17, 18, 21, 22, 26, 51, 54, 63, 65, and 66 were rejected as not enabled, because they encompassed HPV-16 and the HPV-16 available at the time of the invention did not produce the conformational epitopes required by the claims. In earlier prosecution, claims reciting "fragment thereof" had been rejected as not enabled (action mailed 9/8/94), and applicants deleted the "fragment" language from the claims to overcome that grounds of rejection (response filed 6/16/1995). After interference proceedings and appeal at the Federal Circuit, it was ordered that applicants are not entitled to a patent containing claims 1-3, 12-14, 16, 19, 23-25, 46, 47, 50, 52, 53, 55-60, 62, and 64.

In the amendment of 9/10/2007, all previously pending claims were cancelled, and new claims 67-91 were filed.

New claims 67-73, 75-86, 88-91 are rejected on the grounds of interference estoppel, being patentably indistinct from the claims lost in interference 104776. The previous claims recited language such as "reproduces the antigenicity and exhibits the same conformation as an L1 major capsid protein expressed on the surface of intact human papillomavirus virions." This covers essentially the same subject matter as the

current language "includes conformational epitopes present on L1 protein on the surface of intact human papillomavirus virions." The current claims explicitly exclude the presence of L2; this does not distinguish from the previous claims, which did not explicitly or implicitly require the presence of L2. Since the claims are not patentably distinct from the lost claims in the interference, applicant is barred from obtaining a patent on these claims. See *In re Deckler,* 24 USPQ2d 1448.

Claim Rejections - 35 USC § 112

Claims 67, 69-77, 79-91 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for L1 protein, does not reasonably provide enablement for fragments of L1 including conformational epitopes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification provides no guidance on how to make fragments of the L1 protein that include conformational epitopes. Much post-filing research has been performed on the nature of HPV conformational epitopes, which indicates that they frequently involve complex interactions between multiple loops formed during the process of folding the L1 protein and assembly into capsomers and higher-order particles. See for example Orozco et al (Journal of Virology 79:9503-9514, 2005) and Carter et al (Journal of Virology 77:11625-11632, 2003). Later work also demonstrated unpredictable effects of truncations and deletions upon papillomavirus L1 assembly and immunological properties. See for example Li et al (Journal of Virology 71:2988-2995,

1997), Paintsil et al (Virology 223:238-244, 1996), Chen et al (Journal of General Virology 79:2137-2146, 1998), Bishop et al (Virology Journal 4:3, 2007), and Chen et al (Molecular Cell 5: 557-567, 2000). Considering the state of the art on the filing date in 1994, the absence of direction in the specification regarding conformational epitope-bearing fragments, the contemporary inability to predict the effects of any mutation upon the formation of conformational epitopes, and the scope of working examples limited to full-length L1 protein, it is concluded that undue experimentation would have been required to enable the full scope of the invention as claimed.

Claims 67, 69-77, 79-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "written description" rejection directed at the "fragment" which "includes conformational epitopes present on L1 protein on the surface of intact human papillomavirus virions." These claims are drawn to a genus of products, specifically HPV L1 protein and fragments of HPV L1 protein which include conformational epitopes. At the filing date of this application, there was little or no information known in the art regarding what portions of the L1 primary sequence contributed to conformational epitopes, and little or no information regarding the folding of the L1 protein so as to create the conformational epitopes. Later research, discussed in more detail above, indicated that truncation and mutation of the primary sequence had unpredictable effects upon the assembly of the L1 protein into higher-

order structures, and upon the formation of conformational epitopes. The specification shows reduction to practice of one species of L1 protein, the full-length species. The specification provides no particular guidance to one seeking to correlate the structure of the L1 protein to the functional formation of conformational epitopes. Therefore, it is concluded that the specification does not reasonably convey that applicants possessed the claimed genus of fragments.

Priority

This application has an actual filing date of 3/22/1994, and claims benefit to the 6/25/1992 filing date of application 07903109, as a continuation.

As of the actual filing date of 3/22/1994, the papillomavirus art was cognizant of a wild-type species of HPV16 L1 protein which inherently possessed the conformational epitopes of intact virions, see for example Kirnbauer et al (Journal of Virology 67:6929-2936, December 1993). See also Kirnbauer et al (Journal of the National Cancer Institute 86:494-499, 1994) which provides evidence that the prototype HPV16 L1, in common use before 1994, lacked conformational epitopes and the wild-type HPV16 L1 possessed conformational epitopes. See particularly page 497, column 1.

In 1992, the papillomavirus art was not aware that the sequence of HPV16 in common use did not produce an L1 protein that includes conformational epitopes of intact virions. Since neither common knowledge in the art nor the teachings in the specification describe or enable the particular requirements for HPV16 in 1992, benefit of the priority date is denied for claims 74, 84, and 87.

Since the state of the art on the actual filing date of 3/22/1994 included knowledge of a species of HPV16 L1 that inherently included conformational epitopes, claims 74, 84, and 87 are not rejected here on the basis of inadequate description or enablement for the HPV16 species.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 74, 84, and 87 are rejected under 35 U.S.C. 102(a) as being anticipated by Kirnbauer et al (Journal of Virology 67:6929-2936, December 1993). As discussed above, applicants are denied the benefit of the filing date of the parent application for these claims. Kirnbauer teaches HPV16 products which inherently include conformational epitopes present on the L1 surface of intact papillomavirus virions. Since the HPV16 L1 products are the only components of the vaccines of claims 84 and 87, Kirnbauer anticipates these claims as well.

Claims 74, 84, and 87 are rejected under 35 U.S.C. 102(e) as being anticipated by Lowy et al 5716620 or 5871998, see the claims. As discussed above, applicants are denied the benefit of the filing date of the parent application for these claims. Lowy's

effective date for the patent claims is March 16, 1993, which is prior to applicant's effective filing date for these claims.

Inventorship

In view of the papers filed 11/15/2006, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of inventor Shin-Je Ghim.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher whose telephone number is 571-272-0906. The examiner can normally be reached on varying dates and times; please leave a message.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
Primary Examiner, Art Unit 1648

3/13/09